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EXAMINER	
COOK, LISA V	

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1641	

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23

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/679,043	Applicant(s) SUNDREHAGEN ET AL.	
	Examiner Lisa V. Cook	Art Unit 1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 September 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *28-49* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *28-49* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Continued Examination

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 17 September 2003 has been entered.

Preliminary Amendment

2. In response to Applicant's preliminary amendment-D, (filed 9/17/3 Paper #22) Claims 1-27 were canceled without prejudice or disclaimer. New claims 28-49 were added. Accordingly claims 28-49 are pending and under consideration.

OBJECTIONS MAINTAINED

Information Disclosure Statement

3. The listing of references in the specification is not a proper information disclosure statement. 37 CFR 1.98(b) requires a list of all patents, publications, or other information submitted for consideration by the Office, and MPEP § 609 A(1) states, "the list may not be incorporated into the specification but must be submitted in a separate paper." Therefore, unless the examiner on form PTO-892 or applicant on PTO-1449 has cited the references they have not been considered.

4. The information disclosure statements filed 1/23/01-Paper #4 and 12/5/01-Paper #10, have been considered as to the merits prior to first action.

Response to Arguments

5. Applicant's arguments with respect to claims 1-27 have been considered but are Moot in view of the new grounds of rejection.

NEW GROUNDS OF REJECTION NECESSITATED BY AMENDMENT

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

6. Claims 28-49 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A. Claims 28 and 49 are vague and indefinite because they both utilize the acronym (holo-TCII) to reference different compounds. Claim 28 identifies holo-TCII as transcobalamin II bound cobalamin, while claim 49 identifies holo-TCII as holo- transcobalamin II. It is suggested the acronym is employed and defined consistently in order to obviate the rejection.

B. Claims 28 and 49 are not clear as to what the immobilized cobalamin will bind. Specifically the claims requires "selective binding", however it is not clear if the cobalamin will bind only apo-forms of TCII, only apo-forms of haptocorrin, or only all forms of haptocorrin. The claims should be re-written to clearly set forth what cobalamin will bind.

C. The terms "analogue or fragment thereof" in claims 28 and 49 are relative terms, which renders the claim indefinite. The terms are not defined by the claims, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. It is not clear as to what if any analogues and or fragments would maintain the binding activity of the immobilized cobalamin. Accordingly the claims are not clear.

D. Claims 28 and 49 are vague and indefinite because it is not clear if the sample that is subsequently contacted with a specific binding ligand for TCII or holo-TCII is the immobilized sample, the non-immobilized sample, or both. Please clarify the claimed method.

E. Claims 28 and 49 are vague and indefinite because a "separation step" or "removal step" between apo-forms of TC II and haptocorrin and holo forms of TC II and haptocorrin is not recited. Applicant argues that the instant invention separates apo and holo complexes. See paper #15, page 4, 4th paragraph. However, as recited the sample is contacted with an immobilized cobalamin which binds apo-forms of TC II and haptocorrin, then the same sample is subsequently contacted with a specific binding ligand for TC II or holo-TC II.

It is not clear as to how the assay will allow for the separation of apo-TC II and apo-haptocorrin when both apo forms and holo forms are present in the reactions mixture. The final detector measure TC II or cobalamin but does not distinguish between apo and holo forms, therein all forms present in the mixture will be detected. Please clarify the separation of apo forms wherein only holo forms remain in the mixture for further detection in the instant claims.

F. Claim 29 is unclear in how the separation being so affected allows for an increased measurement of holo-TCII concentration of at least 3-fold. Moreover, it is unclear when the concentration of the initial sample was determined such that it can be compared. Thus, the claim needs to recite all the necessary method steps required to perform the claimed method.

G. Claim 31 is indefinite for being in improper Markush format. The office recommends the use of the phrase "selected from the group consisting of...." with the use of the conjunction "and" rather than or in listing species. See MPEP 706.03(Y).

H. Claim 35 is vague and indefinite in utilizing the term "if" and parenthesis because it is not clear what Applicants intend to include as claim limitations. It is not clear if the wording after the term "if" and included in parenthesis are apart of the instant claims. The should be removed from the claims.

I. Claim 35 is not clear with respect to what the immobilized ligand and non-immobilized ligands will bind. Please see lines 6-10.

J. Claims 36 and 37 recites the limitation "possesses". This is not clear because it is not known if the ligand binds holo-TCII or some other component.

K. Claim 38 recites that the degree of cross-reactivity is between 0.1% and 1%, while claim 39 requires that the degree of cross-reactivity is less than O.1%. Therefore, there is insufficient antecedent basis for the limitation of claims 39 in claim 38.

L. Claims 38 and 39 recite the limitation "HC". However the acronym has not been defined in the instant claims or utilized previously. Please define.

M. Claim 43 is indefinite for being in improper Markush format. The office recommends the use of the phrase "selected from the group consisting of...." with the use of the conjunction "and" rather than or in listing species. See MPEP 706.03(Y). Further the claim utilizes open language (comprising). Does the claim read on the body fluid samples listed or any and al body samples?

N. Claims 28-49 employ various ligands (immobilized/non-immobilized) as well as labeled ligands, specific binding ligands, and binding partners. This is vague and indefinite because it is not clear if all the ligands are the same or if Applicant intends to include multiple ligands. For example, in claim 34 the recitation of a labeled ligand is not clear because claim 28 already includes a ligand bound fraction. Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claim 31 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claims contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a written description rejection.

Claim 31 is drawn to specific binding ligands or TC 11 or holo-TC 11. The claim includes several types of ligand possibilities, which are not presented in the specification. The only specific binding ligand for TCII taught in the specification is anti-TC11 antibodies. Therefore only anti-TCIIs are enabled by the specification. Specific binding ligands such as polypeptides, oligopeptide, small organic chemical, binders from combinatorial chemistry libraries or phage display library or specifically binding sequences of DNA and RNA have not been described as being capable of determining holo-TC11 in the manner claimed by claim 31.

The specification does not teach making specific binding ligands such as like polypeptide, oligopeptide, small organic chemical, binders from combinatorial chemistry libraries or phage display library or specifically binding sequences of DNA and RNA that only bind to TC 11 For instance, there is no disclosure of peptides, small organic chemicals or sequences that preferentially bind TC 11. Absent factual evidence that the recited ligands will bind TC 11, it is not deemed unreasonable that one skilled in the art would know how the claimed ligands would bind to TC 11. This has been determined in light of the specifications lack of written description. Moreover, the specification recites a range of binding ligands without any specificity to TCII. When the suspension is used for targeting selected cells or tissues the TCII binding ligand should contain molecules selective to bind the marker of interest. (page 8 paragraph 3/4). It is known that monoclonal antibodies and associated antibody fragments directed to epitopes on TCII can act as specific binding ligands.

However, there is no evidence that specific binding ligands such as polypeptides, oligopeptide, small organic chemical, binders from combinatorial chemistry libraries or phage display library or specifically binding sequences of DNA and RNA without any specific binding regions specific to TC 11 have been identified and further, will perform in the assay. Thus, the specification fails to adequately describe such binding ligands. Therefore the recitation of a specific binding ligand without specific regions or sequences directed specifically to TCII will result in an unpredictable use and therefore unreliable correspondence between the broadly claimed specific binding ligands and the indicated anti-TC11 antibodies disclosed in the specification having known specific binding affinity to TCII; therefore the claimed specific binding ligands lack support regarding utility and/or enablement.

Absent clear demonstration of the production of specific binding ligands such as polypeptides, oligopeptide, small organic chemical, binders from combinatorial chemistry libraries or phage display library or specifically binding sequences of DNA and RNA which specifically and preferentially bind TC 11, the recited specific binding ligands could not be used in any manner for the determination of holo-TC11 in a body sample comprising the recited steps.

In the absence of further guidance from Applicants, it is clear that applicants were not in possession of the specific binding ligands, which are not monoclonal antibodies. *Vas-Cath Inc. U. Mahurkar, 19 USPQ2d1111*, make clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention.

The invention is, for purposes of the written description inquiry, whatever is now claimed." (See page 1 1 17). The specification does not "clearly allow persons of ordinary skill in the art to recognize that (he or she) invented what is claimed." (See Vas-Cath at page 1117). The specification only discloses antibodies as being appropriate binding ligands and there is no disclosure of any other specific binding ligands. Therefore, conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method for determining sequence identity. Adequate written description requires more than a mere statement that it is part of the invention and a reference to a potential method of expression. See *Fiers e. Revel*, 25 USPQ 2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. V. Chugai Pharmaceutical Co. Lts.*, 18 USP2Zd 1016.

Thus a skilled artisan cannot envision all the contemplated specific binding ligands and therefore conception cannot be achieved until reduction to practice has occurred. Furthermore, In *The Reagents of the University of California v. Eli Lilly,* (43USP2Zd 1398-1412), the court held that a generic statement which defines a genus of nucleic acids does not provide an adequate written description of the genus. Applicants are not required to disclose every species encompassed by a genus, thus the description of a genus is achieved by the recitation of a representative number species, falling within the scope of the claimed genus. At section B(1), the court states that "An adequate written description of a nucleic acid molecule...'requires a precise definition, such as by structure, formula, chemical name, or physical properties'".

Therefore, the claims lack written description of the specific binding ligands. In view of the lack of written description of the claims and the lack of written description, the full breadth of the claims fail to meet the written description provision of 35 USC 1 12, first paragraph.

Double Patenting

8. Double patenting obviousness-type rejection:

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

9. Claims 28-49 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 54-72 of U.S. Application No. 09/417,226. Although the conflicting claims are not identical, they are not patentably distinct from each other because both inventions are drawn to holo-TC11 analysis procedures. This invention is encompassed within Application #09/417,226. This is a provisional obvious-type double patenting rejection because the conflicting claims have not in fact been patented.

Claim Rejections - 35 USC § 103

10. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negative by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

I. Claims 28-35, 43, 44, and 49 are rejected under 35 U.S.C. 103(a) as being obvious over Herbert (US Patent #4,680,273) in view of Maggio (Immunoenzyme technique I, CRC press © 1980, pages 186-187).

Herbert discloses various assays to measure transcobalamin II bound cobalamin. See column 3 – column 6. In one instance applicable assays wherein a body sample is contacted with labeled vitamin B12, therein allowing the cobalamin in the sample and labeled cobalamin to compete for binding to a binding ligand. The amount of bound verse free vitamin B_{12} or cobalamin was used to identify the amount of vitamin B_{12} or cobalamin present in the sample.

See column 1 lines 12-41. The detection of vitamin B_{12} or cobalamin is subsequently employed to determine the vitamin B_{12} carried by transcobalamin II (holo-TC II) in the sample (holo-TCII). This reads on Applicant's claims directed to the measurement of holo-TCII via cobalamin. Although Herbert does not specifically recite that cobalamin selectively binds apo-forms of TCII and haptocorrin, it is noted that the use of cobalamin would necessitate the same binding characteristics noted by Applicant.

Specifically, Herbert teaches a method of determining the amount vitamin B12 or cobalamin in a sample. Holo-TCII or TCII containing bound vitamin Bl2 is taught in column 2 lines 29-31. The sample can be a cell free sample, like serum (blood extracted fluid free from solid elements) and can detect Vitamin B12 carried by TCII (holo-TCII) at levels as low as 15pg/ml. Therein reading on applicants 9pM or 9pg/l – claim 30. See column 6 lines 37-47 for example. In table I in column 7 lines 30-49 at least a three fold increase over deficient patients is exhibited as required by claim 29. The assay for vitamin B_{12} is accomplished by using a binder specific for cobalamins (column 5 lines 10-15). In an immunoassay the binder can be a monoclonal or polyclonal antibody, a tracer is also used which can be vitamin B_{12} or an appropriate analog that is labeled with a detectable marker (column 5 lines 16-30). The binder can be in either supported or unsupported form, and in the instances where the binder is supported, it can be supported by a solid support and the bound free fractions may be separated without the use of a separating agent, while if the binder is unsupported, then the bound free fractions can be separated by using a separating agent (column 5 lines 33-42).

The cobalamin may be determined by providing a blood sample, which contains essentially only TCII. (column 3 lines 3-6). Separation may be conducted via precipitation of TCII, although other methods for separating TCII from a sample are applicable (column 3 lines 40-46).

In one embodiment, TCll can be separated from a sample using selective antibodies (column 3 lines 54-55) where the antibody can be coupled to a solid support to more easily separate TCII (column 3 lines 63-64). At pH=6, TCII binds to sephadex while the other transcobalamin proteins do not (column3 line 65). Once the TCII-vitamin B12 solution is obtained, the resulting solution may be subjected an assay for vitamin B12 where radioassay for vitamin B12 includes the removal of vitamin B12 from TCII complex, for example by heating or the use of hydrochloric acid at pH=2 to destroy the TCII and removal of the B12 (column 4 lines 15-20). Vitamin Bl2 dissociates from TCll when both the ionic strength and pH are low (column 4 lines 35-37). Thus cobalamin can be selectively freed from TCII (column 4 lines 25-26). Binding of additionally haptocorrins are also taught, along with methods of separation and detection (column 3-4).

Although Herbert teaches assay formats including the addition of cobalamin or vitamin B12 to a sample in order to detect holo-TCII (column 1lines 12-61), the patent does not specifically teaching reagent immobilization to a solid support. Particularly the immobilization of cobalamin is not taught.

However, Maggio disclose immunoassays wherein reagents, either the antigen or antibody is immobilized onto a solid phase. The solid phase can be particles, cellulose, polyacrylamide, agarose, discs, tubes, beads, or micro plates (micro titer plates). See page 186.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to immobilize the reagents like cobalamin on a solid support/micro titer plates as taught by Maggio in the assay method to measure holo-TCII of Herbert because Maggio taught that solid supports/micro plates or micro titer plates "are very convenient for reagent immobilization and eliminate washing thereby reducing labor in assay procedures". Page 186, last line.

II. Claims 40-42 are rejected under 35 U.S.C. 103(a) as being unpatentable over Herbert (US Patent #4,680,273) in view of Maggio (Immunoenzyme technique I, CRC press © 1980, pages 186-187) and in further view of Hoyle et al. (US Patent #5,451,508).

Please see Herbert in view of Maggio as set forth above.

Herbert in view of Maggio differ from the instant invention in not specifically teaching various assay configurations including a two recptors/ligands to vitamin B12 (immobilized cobalamin competes with labeled ligand and sample ligand).

However, Hoyle et al. teach a method of assaying vitamin B12 based on competitive binding, which employs a labeled reactant (ligand) as well as the ligand present in the sample of interest. See abstract and column 2 lines 35-63.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to use at least two receptors to vitamin B12 or cobalamin as taught by Hoyle et al. in the assay for bound cobalamin of Herbert in view of Maggio because Hoyle et al. taught that this procedure eliminated false positives, was rapid, and useful in clinical settings. See column 1 line 63 through column 2 line 27.

III. Claims 45-48 are rejected under 35 U.S.C. 103(a) as being unpatentable over Herbert (US Patent #4,680,273) in view of Maggio (Immunoenzyme,technique I, CRC press © 1980, pages 186-187) and in further view of Houts (US Patent #4,465,775).

Please see Herbert in view of Maggio as set forth above.

Herbert in view of Maggio do not teach the known methods of separating bound fractions, labels, or calibrants useful in measuring holo-TCII.

However, Hoyle et al. teach a method of assaying vitamin B12 based on competitive binding, which employs a labeled reactant (ligand) as well as the ligand present in the sample of interest. See abstract and column 2 lines 35-63. See column 1 lines 17-20. The competitive binding assays use proteins which not only bind to B_{12}, but also to cobalamin analogues including transcobalamin11, R proteins and intrinsic factor (IF) present in human sera (column 1 lines 55-66). The assay distinguishes B_{12} from its analogues in order to give a more precise measurement for actual B12. Houts also teaches a comparison of cyanocobalamin and cyanocobalamin-d-iodohistamide in a competitive protein-binding assay (column 5 lines 3-6). A centrifugation step was performed on the supernatants and the tubes were decanted and counted (column 5 lines 19-21).

No more than routine skill is involved in adjusting the amount of a component of a claimed process as stated in the claims. Therefore, neither changes in concentrations nor determining optimum concentrations, which are suitable for materials have been held to involve patentable inventions.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to use the various assay protocols with different reagents, separation, labels, etc. as taught by Houts in the method of Herbert in view of Maggio to perform vitamin B_{12} analysis, because such assays variation as taught by Houts were taught to allowed one to measure B_{12} and account for sample mixtures with interfering binding proteins in order to more precisely measure B_{12}. Column 2 lines 1-30.

One having ordinary skill in the art would have been motivated to do this to acquire the enhanced sensitivity and ability to reduce background fluorescence while providing more data sets for analysis, wherein accurate and precise detection is rapidly available.

IV. Claims 36-37 are rejected under 35 U.S.C. 103(a) as being unpatentable over Herbert (US Patent #4,680,273) in view of Maggio (Immunoenzyme technique I, CRC press © 1980, pages 186-187) and in further view of Hoyle et al. (US Patent #5,451,508).

Please see Herbert in view of Maggio as set forth above.

Herbert in view of Maggio do not teach the specific affinity constants as recited in claims 36-37. However, Hoyle et al employ specific monoclonal antibodies having high affinity constants use in all immunoassays since they are known in the art to increase sensitivity of the immunoassay.

Hoyle et al. teach the use of monoclonal antibodies with affinity constants of at least 5 x 10^9 Mol^{-1}, and most preferably 5 x10^{10}. Figure 2 shows more sensitive antigen determination was achieved with monoclonal antibodies. The affinity properties as recited by the claims are conventional affinities for monoclonal antibodies. Thus, one of skill in the art would desire a high affinity antibody to increase sensitivity of the assay.

11. For reasons aforementioned, no claims are allowed.

Remarks

12. Prior art made of record and not relied upon is considered pertinent to the applicant's disclosure:

A. Allen et al. (US Patent #4,332,785) disclose an immunoassay utilizing immunoreactive proteins like transcobalamin II or transcobalamin II receptor to measure reticulocytes. ((Abstract)

B. Herbert (US Patent #4,680,273) discloses assay methods to measure B12 deficiency.

13. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO fax Center located in Crystal Mall 1. The faxing of such papers must conform to the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The Group 1641 Fax number is (703) 872-9306, which is able to receive transmissions 24 hours/day, 7 days/week.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lisa V. Cook whose telephone number is (571) 272-0816. The examiner can normally be reached on Monday – Friday from 8:00AM – 4:30PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le, can be reached on (571) 272-0823.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to Group TC 1600 whose telephone number is (571) 272-1600.

Lisa V. Cook
Remsen 3C-59
571-272-0816
4/9/04

LONG V. LE
SUPERVISORY PATENT EXAMINER
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04/30/04